REMARKS

Claims 1-9, 12 and 13 presently appear in this case. No claims have been allowed. The Official Action of September 12, 2000, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

The present invention relates to a peptide corresponding to positions 89-96 of the human C-reactive protein (CRP) of the formula: Val_{89}-Thr-Val-Ala-Pro-Val-His-Ile_{96} and modifications thereof obtained by substitution, elongation and amidation of the C-terminal or acylation of the N-terminal. These peptides may be used to inhibit the enzymatic activity of human Leukocyte Elastase (hLE) and/or of human Leukocyte Cathepsin G (hCG) and can be used for the treatment of chronic inflammation conditions such as rheumatoid arthritis, pulmonary emphysema and cystic fibrosis.

Claims 1-8 have been rejected under 35 USC 101 because the claimed invention is directed toward non-statutory subject matter. The examiner states that naturally occurring proteins and peptides are considered non-statutory subject matter. The examiner suggests overcoming the rejection by amending the claims to contain wording such as "an isolated and purified peptide ...".

Claim 1 has now been amended to specify that the peptide is an isolated peptide. Accordingly, it is urged that this rejection has now been obviated.

Claims 1, 2 and 9-13 have been rejected under 35 USC 112, second paragraph, as being indefinite. The examiner states that claim 1 is indefinite in the recitation of "a core peptide corresponding to positions 89-96 of the sequence of human C-

reactive protein (CRP) of the formula ..." as one of skill in the art would not know what is not encompassed by this recitation.

Claim 1 has now been amended to change the term "corresponding to" to read "identical to". Accordingly, this part of the rejection has now been obviated.

The examiner states that claims 10 and 11 are indefinite and fail to comply with 35 USC 101.

By a paper entitled Supplemental Preliminary Amendment filed with the filing of this case on July 29, 1998, claims 10 and 11 were deleted in their entirety. To the extent that this Supplemental Preliminary Amendment may be missing from the record, this paper again deletes claims 10 and 11. Accordingly, this rejection has now been obviated.

Claims 1 and 2 have been rejected under 35 USC 102(b) as being anticipated by Yavin. The examiner states that Yavin teaches that the proteolysis of human CRP by neutrophil derived lysosomal enzymes generates peptides which modulate neutrophil function as well as the implications to the anti-inflammatory mechanism. The examiner states that Yavin teaches isolation of CRP and peptide fractions generated therefrom were assayed for the effect on superoxide ion generation using a cytochrome C assay. The examiner states that while Yavin does not teach that these peptides are capable of inhibiting the enzymatic activity of hLE or hCG, many if not all of these peptides, and particularly the full-length CRP protein itself would have this ability inherently. Thus, the examiner considers that the full length CRP as well as

many additional peptides of Yavin is anticipated by Yavin. This rejection is respectfully traversed.

Claim 1 has now been amended to amend paragraph (ix) to specify that the peptide does not include the entire CRP. Furthermore, the examiner is incorrect that the full length CRP protein will inherently have the ability to inhibit the enzymatic activity of hLE and hCG. The examiner's attention is invited to page 3, line 13, of the present specification which states that CRP as a whole protein was reported to have no inhibitory effect on hLE. As the claim only covers peptides capable of inhibiting *in vitro* the enzymatic activity of hLE and/or hCG, they do not comprehend CRP. In any event, the claims have been amended so that the formula does not comprehend CRP.

With respect to the fragments, none of the fragments isolated by Yavin include the core peptide corresponding to positions 89-96 of CRP. Thus, the present claims do not comprehend any of the fragments disclosed in Table 1 of Yavin. There is nothing in Yavin that would lead anyone to believe that he isolated a peptide that included the core peptide identical to positions 89-96 of human CRP. As the claims now specify "an isolated peptide", they do not comprehend anything in a fraction with a mixture of unspecified fragments. Thus, no fragment within the scope of claim 1 is anticipated by Yavin. The examiner has not explained why any such fragment might be obvious to one of ordinary skill in the art reading Yavin. The examiner concedes that Yavin does not teach that these peptides are capable of inhibiting *in vitro* the enzymatic activity of hLE and/or hCG.

Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 1 and 2 have been rejected under 35 USC 102(b) as being anticipated by Shephard. The examiner states that Shephard teaches the isolation of CRP and peptide fractions generated from CRP by lysosomal enzyme digestion. The examiner states that Shephard was in possession of the full length CRP as well as many additional peptides that meet the limitation of claim 1(ix) reciting a peptide obtained by elongation of a peptide of (i)-(viii) at the N-end or C-terminal. This rejection is respectfully traversed.

Claim 1 as presently amended is not anticipated or made obvious by Shephard for the same reasons as discussed above with respect to Yavin. None of the fractions specifically identified in Shephard contain the core peptide identical to positions 89-96 of CRP. Every peptide covered by claim 1 (ix) has this core. Accordingly, none of the sequences of Shephard anticipate the present claims. There is no indication that Shephard isolated any other sequence, let alone one including the core peptide required by the present claims. Furthermore, it would not be obvious to isolate any other peptides as Shephard indicates that the fragments in all those fractions possessing superoxide ion formation inhibition activity have been isolated and identified. Accordingly, none of the claims are anticipated or made obvious by Shephard. Reconsideration and withdrawal of this rejection are also respectfully urged.

Claims 9-13 have been rejected under 35 USC 103(a) as being unpatentable over Yavin and claims 9-13 have also been rejected under 35 USC 103(a) as being unpatentable over Shephard. The examiner states that one of ordinary skill in the art would have been motivated to create a pharmaceutical composition of the peptides disclosed in Yavin or Shephard. These rejections are respectfully traversed.

As discussed hereinabove, neither Yavin nor Shephard disclose any peptides falling within the scope of claim 1 and claim 1 is patentable over Yavin and Shephard. Accordingly, it must follow that the composition of claim 9 and the methods of claims 12 and 13 must also be patentable over Yavin or Shephard as the active agent used in each is not disclosed or made obvious by Shephard. Reconsideration and withdrawal of these rejections are therefore also respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By _____
ROGER L. BROWDY
Registration No. 25,618

RLB:al
624 Ninth Street, N.W.
Washington, D.C. 20001
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
F:\,Y\YEDA\Fridkinl\pto\AmendmentD.doc